

What is claimed is:

- 1           1.       An injectable pharmaceutical composition comprising:  
2           an aqueous suspension of microdroplets suitable for intravenous delivery, the  
3           microdroplets having a mean diameter between 200 Angstroms and one micron, the  
4           microdroplets comprising a substantially water-insoluble, pharmacologically acceptable  
5           liquid, a camptothecin dissolved in the water-insoluble, pharmacologically acceptable liquid,  
6           and an outer layer comprising a phospholipid.
- 1           2.       An injectable pharmaceutical composition according to claim 1 wherein the  
2           camptothecin is selected from the group consisting of 9-nitro-20(S)-camptothecin, 9-amino-  
3           20(S)-camptothecin, 9-methyl-camptothecin, 9-chloro-camptothecin, 9-flouro-camptothecin,  
4           7-ethyl camptothecin, 10-methyl-camptothecin, 10-chloro--camptothecin, 10-bromo-  
5           camptothecin, 10-fluoro-camptothecin, 9-methoxy-camptothecin, 11-fluoro-camptothecin, 7-  
6           ethyl-10-hydroxy camptothecin, 10,11-methylenedioxy camptothecin, and 10,11-  
7           ethylenedioxy camptothecin, and 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy  
8           camptothecin.
- 1           3.       An injectable pharmaceutical composition according to claim 1 wherein the  
2           camptothecin is selected from the group consisting of 9-nitro-20(S)-camptothecin, 9-amino-  
3           20(S)-camptothecin, 7-ethyl-10-(4-(1-piperdino)-1-piperdino)-carbonyloxy-camptothecin, 7-  
4           ethyl-10-hydroxy-20(S)-camptothecin, 10,11-methylenedioxy-20(S)-camptothecin, 9-chloro-  
5           20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, and 11-  
6           hydroxy-20(S)-camptothecin.
- 1           4.       An injectable pharmaceutical composition according to claim 1 wherein the  
2           camptothecin is 9-nitro-20(S)-camptothecin.
- 1           5.       An injectable pharmaceutical composition according to claim 1 wherein the  
2           pharmaceutical composition has a pH less than 7.
- 1           6.       An injectable pharmaceutical composition according to claim 1 wherein the  
2           pharmaceutical composition has a pH less than 6.

1           7.       An injectable pharmaceutical composition according to claim 1 wherein the  
2       pharmaceutical composition has a pH between 5 and 6.

1           8.       An injectable pharmaceutical composition according to claim 1 wherein the  
2       pharmaceutical composition comprises an isotonic solution.

1           9.       An injectable pharmaceutical composition according to claim 1 wherein the  
2       pharmaceutical composition comprises mannitol or trehalose.

1           10.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       composition has been thermally sterilized.

1           11.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       composition has been thermally sterilized by heating to at least 121°C for at least 15  
3       minutes.

1           12.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       pharmaceutically acceptable organic liquid is selected from the group consisting of alkanes,  
3       dialkyl ethers, long-chain esters, hydrophobic esters, biocompatible silicones, biocompatible  
4       high molecular weight fluorocarbons, oil-soluble vitamins and volatile liquid anesthetics.

1           13.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       camptothecin is present in amounts of up to about 25% w/w.

1           14.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       camptothecin is present in amounts of from about 0.05% w/w to about 5% w/w.

1           15.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       camptothecin is present in amounts of from about 0.1% w/w to about 1% w/w.

1           16.      An injectable pharmaceutical composition according to claim 1 wherein the  
2       camptothecin is present in amount of about 0.2% w/w.

1           17.     An injectable pharmaceutical composition according to claim 1 wherein the  
2     camptothecin is present in amounts of up to about 5% w/w.

1           18.     An injectable pharmaceutical composition comprising:  
2             a dispersion in an aqueous carrier solution comprising one or more pharmaceutically  
3     acceptable tonicity modifier agents and liquid droplets of micrometer to submicrometer, the  
4     droplets comprising  
5             a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid vehicle  
6             a camptothecin dissolved in the lipophilic liquid vehicle, and  
7             an outer layer surrounding the droplet comprising at least one membrane-forming  
8     amphipathic lipid,  
9             wherein upon thermal sterilization the dispersion does not aggregate, flocculate,  
10    agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted  
11    mean diameter of 10  $\mu$ m.

1           19.     An injectable pharmaceutical composition comprising:  
2             an aqueous carrier solution comprising one or more pharmaceutically acceptable  
3     tonicity modifier agents;  
4             a dispersion of liquid droplets of a first size distribution, the liquid droplets  
5     comprising  
6             a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid  
7     vehicle,  
8             solid particles of a camptothecin of a second size distribution, and  
9             an outer layer surrounding the droplet comprising at least one membrane-  
10    forming amphipathic lipid;  
11             wherein the first size distribution is in the range of submicrometer to micrometers,  
12    and the second size distribution is smaller than the first size distribution; and  
13             wherein upon thermal sterilization, the dispersion does not aggregate, flocculate,  
14    agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted  
15    mean diameter of 10  $\mu$ m.

1           20.     An injectable pharmaceutical composition according to claim 18 wherein the  
2     membrane-forming amphipathic lipid comprises a phospholipid.

1           21.     An injectable pharmaceutical composition according to claim 20 wherein the  
2 phospholipid is selected from the group consisting of saturated phospholipids, unsaturated  
3 phospholipids, synthetic phospholipids, natural phospholipids, and combinations thereof.

1           22.     An injectable pharmaceutical composition according to claim 20 wherein the  
2 phospholipid is selected from the group consisting of natural and synthetic lipids, hen egg-  
3 derived phospholipid, egg phospholipid, purified egg phospholipid, soy phospholipid,  
4 dimyristoyl lecithin, didodecanoyl lecithin, dioleoyl lecithin, dilinoleoyl lecithin, alpha-  
5 palmito-beta-oleoyl lecithin, alpha-palmitoyl-beta-linoleoyl lecithin, alpha-oleoyl-beta-  
6 palmitoyl lecithin, diarachidonoyl lecithin, alpha-palmito-beta-myristoyl lecithin, dimyristoyl  
7 phosphatidic acid, dipalmitoyl phosphatidic acid, distearoyl phosphatidic acid, phosphatidyl  
8 serine, phosphatidyl inositol, dimyristoyl phosphatidyl glycerol, dipalmitoyl phosphatidyl  
9 glycerol, dioctadecanoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl ethanolamine,  
10 dihexadecyl phosphatidyl ethanolamine, dilauryl phosphatidyl ethanolamine, dimyristoyl  
11 phosphatidyl ethanolamine, dipalmitoyl phosphatidyl ethanolamine, Lipoid E80, Lipoid ES,  
12 Lipoid 90H, and Lipoid 100H.

1           23.     An injectable pharmaceutical composition according to claim 20 wherein the  
2 phospholipid comprises Lipoid E80.

1           24.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 outer layer further comprises cholesterol.

1           25.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 membrane-forming amphipathic lipid is present in amounts of from 0.2% w/w to about 5%  
3 w/w.

1           26.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 membrane-forming amphipathic lipid is present in amounts of from 1% w/w to about 5%  
3 w/w.

1           27.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 membrane-forming amphipathic lipid is present in amounts of about 4% w/w.

1           28.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 lipophilic liquid vehicle is selected from the group consisting of vegetable oils, animal oils,  
3 synthetic oils, semi-synthetic oils, soybean oil, medium chain triglycerides, long chain  
4 triglycerides, triglycerides of C8 to C12 saturated fatty acids, triglycerides of C14 to C22  
5 saturated fatty acids, triglycerides of C14 to C22 unsaturated fatty acids, and combinations  
6 thereof.

1           29.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 lipophilic liquid vehicle is selected from the group consisting of soybean oil, triglycerides of  
3 C8 to C12 saturated fatty acids, and combinations thereof.

1           30.     An injectable pharmaceutical composition according to claim 18 wherein the  
2 lipophilic liquid and the membrane-forming amphipathic lipid further comprise cholesterol.